

### Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claim 1 has been amended, claims 3-5 have been cancelled without prejudice, and new claims 10-21 have been added. Descriptive support for new claims 10 and 11 appears in the first full paragraph on page 30 and the third full paragraph on page 35, respectively; descriptive support for new claims 12-14 appears in the first full paragraph on page 34; and descriptive support for new claims 15 and 16 appears in the first full paragraph on page 30. New claim 17 finds descriptive support in original claim 3 (i.e., claim written in independent form), and new claims 18-21 find descriptive support in original claims 4 and 6-8, respectively. Claims 1, 2, and 6-21 are pending.

The objection to the specification is overcome by the above amendments. Although applicants disagree with the assertion made by the U.S. Patent and Trademark (“PTO”), the present claim language is clearly supported by the first full paragraph on page 30, along with the disclosure of the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184.

The objections to claims 1 and 5 are overcome by the above amendments and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support is respectfully traversed.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) (“[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.”). Hence, the PTO must demonstrate *why* the disclosure is insufficient.

The Federal Circuit has clearly espoused that *per se* conclusions of written description violations cannot be founded upon the basis of genus size alone. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1326-27, 63 USPQ2d 1609, 1614-15 (Fed. Cir. 2002) (refusing to adopt position that three species as a matter of law cannot satisfy written description requirement for significantly larger genus). Thus, the PTO’s conclusion

cannot be based on genus size alone. But that is precisely what the PTO has done at pages 3-4 of the outstanding office action. Because the PTO's position is unsupported by law and unsupported by any facts other than genus size, applicants submit that the PTO's position cannot be sustained.

In contrast, applicants present Exhibits 1-3 (attached hereto) as evidence that the nucleic acid sequence of SEQ ID NO: 183 and the corresponding amino acid sequence of SEQ ID NO: 184 represent the claimed genus. Exhibit 1 is a presentation of a Genbank accession for a thermophilic *Bacillus*, or *Geobacillus*, *polC* nucleic acid that is homologous to the nucleotide sequence of SEQ ID NO: 183. This *polC* nucleic acid was identified by a protein-protein BLAST search of the Genbank database performed using the amino acid sequence of SEQ ID NO: 184 and the BLAST default settings. Homologous sequences were identified in a number of *Bacillus* species, including from the thermophile *Geobacillus kaustophilus* (Exhibit 1). Based upon alignments performed using Align<sup>®</sup> for nucleic acids and ClustalW for amino acids (using the European Molecular Biology Laboratory server and its default settings), this homolog shares about 99 percent identity at the nucleic acid level (Exhibit 2) and about 99 percent identity at the amino acid level (Exhibit 3). Thus, species of PolC subunits from thermophilic organisms that belong to the biological classification *Bacillus*, or *Geobacillus*, clearly share similar structure and, therefore, function.

Applicants submit that the language recited in claims 1 and 9 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, but merely described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only the one rat species disclosed), and the larger genus of 'vertebrate' cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Bacillus* or *Bacillus stearothermophilus*) and the specification describes one or more species within that genus. Claims 1 and 9 recite the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claims 1 and 9 (and claims dependent thereon) find written descriptive support in the present application.

It should be noted that the “Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, ‘Written Description’ Requirement,” make explicitly clear that the description of a representative number of species does *not* require the description to be of such a nature that it would provide support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Hence, the absence of sequences (in the present specification) for the later-identified *polC* and PolC homologs is irrelevant to the issue of whether the present specification provides adequate written descriptive support for their use in accordance with the present invention.

Moreover, the conclusion by the PTO is contrary to evidence submitted herewith by applicants. As demonstrated by Exhibits 1-3, one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because persons of skill in the art would have expected sufficiently related thermophilic organisms from the genus *Bacillus* (and now *Geobacillus*) to possess homologous *polC* nucleotide sequences or thermostable PolC subunit proteins. Exhibits 1-3 confirm this expectation to have been reasonable.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 is improper and should be withdrawn.

The rejection of claims 1-9 under 35 U.S.C. §112 (first paragraph) for lack of enablement is respectfully traversed.

It is the position of the PTO that the specification does not provide sufficient guidance for making and using other DNA molecules (encoding PolC subunit proteins) within the scope of the claims. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Bacillus* (now *Geobacillus*) *stearothermophilus polC* (e.g., SEQ ID NO: 183) and describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 41, line 9 to page 42,

line 29), express the PolC subunit encoded by such homologous *polC* sequences (*see* Example 18, expressing *A. aeolicus* alpha subunit), and test the encoded alpha subunit for Pol III assembly competence (*see* Example 25, testing *A. aeolicus* polymerase assembly with clamp loader) and for polymerase activity (*see* Examples 26 and 30, testing *A. aeolicus* polymerase activity). Thus, one of ordinary skill in the art would have been fully able to make and use DNA molecules and their encoded proteins within the scope of the presently claimed invention.

Moreover, with regard to method 3 for homolog identification, described at page 42, that is precisely the approach used to identify the *polC* homolog shown in Exhibit 1. For this reason, it should be apparent that the present application fully enables the production and use of other species of *Bacillus* or *Bacillus* (now *Geobacillus*) *stearothermophilus polC* homologs.

In view of all of the foregoing, applicants submit that the rejection of claims 1-9 for lack of enablement is improper and should be withdrawn.

Because 1 is allowable for the reasons noted above, applicants further submit that new claims 10-16 also are allowable. Consistent with the PTO acknowledgments at pages 3-4 the outstanding office action, applicants further submit that that the specification provides written descriptive support for and enables the claimed DNA molecules that encode the PolC subunit including the amino acid sequence of SEQ ID NO: 184 (i.e., claims 17-21).

In view of all of the foregoing, applicant submits that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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## **Exhibit 1**



PubMed

Nucleotide

Protein

Genome



Structure

PMC

Taxonomy

OMIM

My NCBI

[Sign In] [Register]

Books

Search Nucleotide

for

Limits

Preview/Index

History

Clipboard

Go

Clear

Details

Display GenBank(Full)

Show 5

Send to

Range: from 1271567

to 1275901

Show whole sequence

☐ Reverse complemented strand Fe☐ 1: BA000043. Reports *Geobacillus kaust...*[gi:56378377]

Features Sequence

Links

LOCUS BA000043 4335 bp DNA linear BCT 04-DEC-2004  
 DEFINITION *Geobacillus kaustophilus* HTA426 DNA, complete genome.  
 ACCESSION BA000043 REGION: 1271567..1275901  
 VERSION BA000043.1 GI:56378377  
 KEYWORDS .  
 SOURCE *Geobacillus kaustophilus* HTA426  
 ORGANISM *Geobacillus kaustophilus* HTA426  
 Bacteria; Firmicutes; Bacillales; Bacillaceae; *Geobacillus*.  
 REFERENCE 1  
 AUTHORS Takami,H., Takaki,Y., Chee,G.J., Nishi,S., Shimamura,S., Suzuki,H.,  
 Matsui,S. and Uchiyama,I.  
 TITLE Thermoadaptation trait revealed by the genome sequence of  
 thermophilic *Geobacillus kaustophilus*  
 JOURNAL (er) Nucleic Acids Res. 32 (21), 6292-6303 (2004)  
 PUBMED 15576355  
 REFERENCE 2 (bases 1 to 4335)  
 AUTHORS Takami,H., Takaki,Y. and Chee,G.  
 TITLE Direct Submission  
 JOURNAL Submitted (25-JUN-2003) Hideto Takami, Japan Marine Science and  
 Technology Center, Microbial Genome Analysis Research Group; 2-15  
 Natsushima-cho, Yokosuka, Kanagawa 237-0061, Japan  
 (E-mail:takamih@jamstec.go.jp,  
 URL:http://www.jamstec.go.jp/jamstec-e/bio/exbase.html,  
 Tel:81-46-867-9643, Fax:81-46-867-9645)  
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## ORIGIN

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```

//

Disclaimer | Write to the Help Desk  
NCBI | NLM | NIH

Aug 15 2006 13:27:38



## Exhibit 2

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#####
# Program: needle
# Rundate: Wed Aug 23 22:03:02 2006
# Align_format: srspair
# Report_file: /ebi/extserv/old-work/needle-20060823-22025746567743.output
#####
```

```
#=====
#
# Aligned_sequences: 2
# 1: SEQ_183
# 2: G_kaustophilus
# Matrix: EBLOSUM62
# Gap_penalty: 10.0
# Extend_penalty: 0.5
#
# Length: 4335
# Identity: 4284/4335 (98.8%)
# Similarity: 4284/4335 (98.8%)
# Gaps: 34/4335 ( 0.8%)
# Score: 25976.0
#
#
#=====
```

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G_kaustophilu	1	atgatgttgagaggggaacaaacggacgtcatggtgacaaaagagcaaaa	50
SEQ_183	21	AGAGCGGTTTCTCATCTGCTTGAGCAGCTGAAGATGACGTCGGACGAAT	70
G_kaustophilu	51	agagcgggtttctcatctgcttgagcagctgaagatgacgtcggacgaat	100
SEQ_183	71	GGATGCGCATTTTCGTGAGGCAGCCATTGCGAAAGTCGTGATCGATAAA	120
G_kaustophilu	101	ggatgccgcattttcgtgagggcagccattcgcaaagtcgtgatcgataaa	150
SEQ_183	121	GAGGAGAAAAGCTGGCATTTTTATTTTCAGTTTCGACAACGTGCTGCCGGT	170
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G_kaustophilu	801	gaccatgaaaatcaccgattacacgaactcgatttttagtcaaaatgttct	850
SEQ_183	821	CGCGCGACAAAGAGGACGCCGAGCTTATGAGCGCGCTCAAAAAAGGCATG	870
G_kaustophilu	851	cgcgcgacaaagaggacgccgagctcatgagcggcgctcaaaaaaggcatg	900
SEQ_183	871	TGGGTGAAAGTGCGCGGCAGCGTGCAAAACGATACGTTTCGTCCGTGATTT	920
G_kaustophilu	901	tgggtgaaagtgcgcggcagcggtgcaaaacgatacgttcgtccgtgattt	950
SEQ_183	921	GGTCATCATCGCCAACGATTGTAACGAAATCGCCGCAAACGAACGGCAAG	970
G_kaustophilu	951	ggtcatcatcgccaacgatttgaacgaaatcgccgcaaacgaacggcaag	1000
SEQ_183	971	ATACGGCGCCGGAAGGGGAAAAGAGGGTCGAGCTCCATTTGCATACCCCG	1020
G_kaustophilu	1001	atacggcgccggaaggggaaaaaagggtcgagctccatttgcataccccg	1050
SEQ_183	1021	ATGAGCCAAATGGACCGGGTCACCTCGGTGACAAAACCTCATTGAGCAAGC	1070
G_kaustophilu	1051	atgagccaaatggacgggtcacctcggtgacaaaactcattgagcaagc	1100
SEQ_183	1071	GAAAAAATGGGGGCATCCGGCGATCGCCGTCACCGACCATGCCGTTGTTC	1120
G_kaustophilu	1101	gaaaaaatgggggcatccggcgatcgccgtcaccgaccatgccgttggttc	1150
SEQ_183	1121	AGTCGTTTCCGGAGGCCTACAGCGCGCGGAAAAACACGGCATGAAGGTC	1170
G_kaustophilu	1151	agtcgtttccggaggcctacagcgcgcgaaaaaacacggcatgaaggtc	1200
SEQ_183	1171	ATTTACGGCCTTGAGGCGAACATCGTCGACGATGGCGTGCCGATCGCCTA	1220
G_kaustophilu	1201	atttacggccttgaggcgaacatcgtcgacgatggcggtgccgatcgcta	1250
SEQ_183	1221	CAATGAGACGCACCGCGCTCTTTTCGGAGGAAACGTACGTCGTCCTTTGACG	1270
G_kaustophilu	1251	caatgaaacgcaccgcgctcttttcggaggaaacgtacgtcgtctttgacg	1300

SEQ_183	1271	TCGAGACGACGGGCCTGTGCGCTGTGTACAATACGATCATTGAGCTGGCG	1320
G_kaustophilu	1301	tcgagacgacgggcctgtcggtgtgtacaatacgatcattgagctggcg	1350
SEQ_183	1321	GCGGTGAAAGTGAAAGACGGCGAGATCATCGACCGATTTCATGTCGTTTGC	1370
G_kaustophilu	1351	gcggtgaaagtgaagacggcgagatcatcgaccggttcattgtcgtttgc	1400
SEQ_183	1371	CAACCCTGGACATCCGTTGTGCGGTGACAACGATGGAGCTGACTGGGATCA	1420
G_kaustophilu	1401	caaccctggacatccgttgtcagtgacaacgatggagctgactgggatca	1450
SEQ_183	1421	CCGATGAGATGGTGAAAGACGCCCCGAAGCCGGACGAGGTGCTAGCCCCGT	1470
G_kaustophilu	1451	ccgatgagatggtgaaagacgccccgaagccggacgaggtgctagcccg	1500
SEQ_183	1471	TTTGTGACTGGGCCGGCGATGCGACGCTTGTGCCCCACAACGCCAGCTT	1520
G_kaustophilu	1501	tttggtgactgggcccggcgatgcgacgcttggtgcccacaacgccagctt	1550
SEQ_183	1521	TGACATCGGTTTAAAAACGCGGCCTCGCTCGCATGGGGCGCGGCAAAA	1570
G_kaustophilu	1551	tgacatcggttttttaaacacgggcctcgctcgcatggggcgcgcaaaa	1600
SEQ_183	1571	TCGCGAATCCAGTCATCGATACGCTCGAGCTGGCCCGTTTATACCCG	1620
G_kaustophilu	1601	tcgcgatccagtcacgatcgctcgagctggcccggtttttatacccg	1650
SEQ_183	1621	GATTGAAAAAACCATCGGCTCAATACATTGTGCAAAAAATTGACATTGA	1670
G_kaustophilu	1651	gatttgaaaaaaccatcggtcaatacattgtgcaaaaaatttgacattga	1700
SEQ_183	1671	ATTGACGCAGCATCACCGGCCATCTACGACGCGGAGGCGACCGGGCATT	1720
G_kaustophilu	1701	attgacgcagcatcaccgcgccatctacgacgaggcgaccgggcatt	1750
SEQ_183	1721	TGCTTATGCGGCTGTTGAAGGAAGCGGAAGAGCGCGGCATACTGTTTCAT	1770
G_kaustophilu	1751	tgcttatgcggtgtgtgaaggaagcggaagagcgcggcatactgtttcat	1800
SEQ_183	1771	GACGAATTAACAGCCGCACGCACAGCGAAGCGTCCTATCGGCTTGCGCG	1820
G_kaustophilu	1801	gacgaattaaacagccgcacgcacagcgaagcgctcctatcggttgcgcg	1850
SEQ_183	1821	CCCGTTCCATGTGACGCTGTTGGCGCAAAACGAGACTGGATTGAAAAATT	1870
G_kaustophilu	1851	cccgttccatgtgacgctgttgcgcaaaaacgagactggattgaaaaatt	1900
SEQ_183	1871	TGTTCAAGCTTGTGTCAATTGTGCGACATTCAATATTTTCACCGTGTGCCG	1920
G_kaustophilu	1901	tgttcaagcttggtgtcattgtcgacacattcaatattttcaccgtgtgccc	1950
SEQ_183	1921	CGCATCCCGCGCTCCGTGCTCGTCAAGCACCGCGACGGCCTGCTTGTCGG	1970
G_kaustophilu	1951	cgcataccgcgctccgtgctcgtaagcaccgcgacggcctgcttgctgg	2000
SEQ_183	1971	CTCGGGCTGCGACAAAGGAGAGCTGTTTGACAACCTTGATCCAAAAGGCGC	2020
G_kaustophilu	2001	ctcgggctgcgacaaaggagagctgtttgacaacttgatccaaaaggcgc	2050
SEQ_183	2021	CGGAAGAAGTCGAAGACATCGCCCCGTTTTTACGATTTTCTGAAGTGCAT	2070
G_kaustophilu	2051	cggaagaagtcgaagacatcgcccgtttttacgattttcttgaagtgc	2100

SEQ_183	2071	CCGCCGGACGTGTACAAGCCGCTCATCGAGATGGATTATGTGAAAAGACGA	2120
G_kaustophilu	2101	 ccgccggacgtgtacaagccgctcatcgagatggattatgtgaaagacga	2150
SEQ_183	2121	AGAGATGATCAAAAACATCATCCGCAGCATCGTCGCCCTTGGTGAGAAGC	2170
G_kaustophilu	2151	 agagatgatcaaaaacatcatccgcagcatcgtcgcccttggtgagaagc	2200
SEQ_183	2171	TTGACATCCCGGTTGTGCGCCACTGGCAACGTCCATTACTTGAACCCAGAA	2220
G_kaustophilu	2201	 ttgacatcccggttgtcgccactggcaacgtccattacttgaacccagaa	2250
SEQ_183	2221	GATAAAATTTACCGGAAAATCTTAATCCATTTCGCAAGGCGGGCGAATCC	2270
G_kaustophilu	2251	 gataaaatttacccgaaaatcttaatccatttcgcaaggcggggcgaatcc	2300
SEQ_183	2271	GCTCAACCGCCATGAACTGCCGGATGTATATTTCCGTACGACGAATGAAA	2320
G_kaustophilu	2301	 gctcaaccgccatgaactgccggatgtatatatttcgtaacgacgaatgaaa	2350
SEQ_183	2321	TGCTTGACTGCTTCTCGTTTMTAGGGCCGGAAAAAGCGAAGGAAATCGTC	2370
G_kaustophilu	2351	 tgcttgactgcttctcgtttttagggccggaaaaagcgaaggaaatcgtc	2400
SEQ_183	2371	GTTGACAACACGCAAAAAATCGCTTCGTTAATCGGCGATGTCAAGCCGAT	2420
G_kaustophilu	2401	 gttgacaacacgcaaaaaatcgcttcgttaatcggcgatgtcaagccgat	2450
SEQ_183	2421	CAAAGATGAGCTGTATACGCCCGCGCATTGAAGGGGCGGACGAGGAAATCA	2470
G_kaustophilu	2451	 caaagatgagctgtatacgcccgcgcatgaagggcgacgaggaaatca	2500
SEQ_183	2471	GGGAAATGAGCTACCGGCGGGCGAAGGAAATTTACGGCGACCCGTTGCCG	2520
G_kaustophilu	2501	 gggaaatgagctaccggcgggcggaaggaaatttacggcgacccggtgccg	2550
SEQ_183	2521	AAACTTGTTGAAGAGCGGCTTGAGAAGGAGCTAAAAAGCATCATCGGCCA	2570
G_kaustophilu	2551	 aaacttgttgaagagcggcttgagaaggagctaaaaagcatcatcggcca	2600
SEQ_183	2571	TGGCTTTGCCGTCATTTATTTGATCTCGCACAAGCTTGTGAAAAAATCGC	2620
G_kaustophilu	2601	 tggctttgccgtcatTTATTTGATCTCGCACAAGCTTGTGAAAAAATCGC	2650
SEQ_183	2621	TCGATGACGGCTACCTTGTCGGGTCGCGCGGATCGGTCGGCTCGTCGTTT	2670
G_kaustophilu	2651	 tcgatgacggctaccttgtcgggtcgcgcgatcggtcggctcgctcgttt	2700
SEQ_183	2671	GTCGCGACGATGACGGAAATCACCGAGGTCAATCCGCTGCCGCCGCATTA	2720
G_kaustophilu	2701	 gtcgcgacgatgacggaaatcacccgaggtcaatccgctgccgccgcatta	2750
SEQ_183	2721	CGTTTGCCCGAACTGCAAGCATTCGGAGTTCTTTAACGACGGTTCAGTCG	2770
G_kaustophilu	2751	 cgtttgcccaaactgcaagcattcggagttctttaacgacggttcagtcg	2800
SEQ_183	2771	GCTCAGGGTTTGATTTGCCGGATAAAAACTGCCCGCGATGTGGGACGAAA	2820
G_kaustophilu	2801	 gctcagggtttgatTTGCCGGATAAAAACTGCCCGCGATGTGGGACGAAA	2850
SEQ_183	2821	TACAAGAAAGACGGGCAAGACATCCCGTTTGAGACGTTTCTCGGCTTTAA	2870
G_kaustophilu	2851	 tacaagaaagacgggcaagacatcccgtttgagacgTTTCTCGGCTTTAA	2900

SEQ_183	2871	AGGCGACAAAGTGCCGGATATCGACTTGAACCTTTTCCGGCGAATACCAGC	2920
G_kaustophilu	2901	 aggcgacaaagtgccggatatcgacttgaacttttcggcggaataccagc	2950
SEQ_183	2921	CGCGCGCCACAACTATACGAAAGTGCTGTTTGGCGAAGACAAACGCTCTAC	2970
G_kaustophilu	2951	 cgcgcgcccaactatacgaaagtgctgtttggcgaagacaacgtctac	3000
SEQ_183	2971	CGCGCCGGGACGATTGGCACGGTCGCTGACAAAACGGCGTACGGATTTGT	3020
G_kaustophilu	3001	 cgcgccgggacgattggcacggtcgctgacaaaacggcgtaaggatttgt	3050
SEQ_183	3021	CAAAGCGTATGCGAGCGACCATAACTTAGAGCTGCGCGCGCGGAAATCG	3070
G_kaustophilu	3051	 caaagcgtatgcgagcgaccataacttagagctgcgcgcgcggaatcg	3100
SEQ_183	3071	A-CGGCTCGCGGCTGGCTGCACCGGGTGAAGCGGACGACCGGGCAGCAT	3119
G_kaustophilu	3101	 acggctcgcggtggctgcacggggtgaagcggaacgacggacagcat	3150
SEQ_183	3120	CCGGGCGGCATCATCGTCGTCGCCGATTATATGGAATTTACGATTTTAC	3169
G_kaustophilu	3151	 ccgggcgcatcatcgctcgctccctgattatatggaaatttacgattttac	3200
SEQ_183	3170	GCCGATTCAATATCCGGCCGATGACACGTCCTCTGAATGGCGGACGACCC	3219
G_kaustophilu	3201	 gccgattcaatatccggccgatgacacgtcctctgaatggcggaacgaccc	3250
SEQ_183	3220	ATTTGACTTCCATTTCGATCCACGACAATTTGTTGAAGCTCGATATTCTC	3269
G_kaustophilu	3251	 atttcgacttccattcgatccacgacaatttgttgaagctcgatattctc	3300
SEQ_183	3270	GGGCACGACGATCCGACGGTCATTTCGCATGCTGCAAGATTTAAGCGGCAT	3319
G_kaustophilu	3301	 gggcacgacgatccgacggtcatttcgcattgctgcaagatttaagggcat	3350
SEQ_183	3320	CGATCCGAAAACGATCCCGACCGACGACCCGGATGTGATGGGCATTTTCA	3369
G_kaustophilu	3351	 cgatccgaaaacgatcccgacgacgacccggatgtgatgggcattttca	3400
SEQ_183	3370	GCAGCACCGAGCCGCTTGGCGTTACGCCGAGCAAATCATGTGCAATGTC	3419
G_kaustophilu	3401	 gcagcaccgagccgcttggcgttacgccgagcaaatacatgtgcaatgtc	3450
SEQ_183	3420	GGCACGATCGGCATTCCGGAGTTTGGCACGCGCTTCGTTCCGCCAAATGTT	3469
G_kaustophilu	3451	 ggcacgatcggcattccggagtttggcacgcgcttcggttcgacaaatgtt	3500
SEQ_183	3470	GGAAGAGACAAGGCCAAAAACGTTTTCCGAACCTCGTGCAAATTTCCGGCT	3519
G_kaustophilu	3501	 ggaagagacaaggccaaaacgttttccgaactcgtgcaaatttccggct	3550
SEQ_183	3520	TGTCGCACGGCACCGATGTGTGGCTCGGCAACGCGCAAGAGCTCATTCAA	3569
G_kaustophilu	3551	 tgtcgcacggcaccgatgtgtggctcggcaacgcgaagagctcattcaa	3600
SEQ_183	3570	AACGGCACGTGTACGTTATCGGAAGTCATCGGCTGCCGCGACGACATTAT	3619
G_kaustophilu	3601	 aacggcacgtgtacgttatcggaagtcacggctgccgcgacgacattat	3650
SEQ_183	3620	GGTCTATTTGATTTACCGCGGGCTCGAGCCGTCGCTCGCTTTTAAATCA	3669
G_kaustophilu	3651	 ggtctatTTGATTTACCGCGGGCTCGAGCCGTCGCTCGCTTTTAAATCA	3700

SEQ_183	3670	TGGAATCCGTGCGCAAAGGAAAAGGCTTAACGCCGGAGTTTGAAGCAGAA	3719
G_kaustophilu	3701		3750
SEQ_183	3720	ATGCGCAAACATGACGTGCCGGAGTGGTACATCGATTTCATGCAAAAAAAT	3769
G_kaustophilu	3751		3800
SEQ_183	3770	CAAGTACATGTTCCCGAAAGCGCACGCCGCCGCCTACGTGTTAATGGCGG	3819
G_kaustophilu	3801		3850
SEQ_183	3820	TGCGCATCGCCTACTTTAAGGTGCACCATCCGCTTTTGTATTACGCGTOG	3869
G_kaustophilu	3851		3900
SEQ_183	3870	TACTTTACGGTGCGGGCGGAGGACTTTGACCTTGACGCCATGATCAAAGG	3919
G_kaustophilu	3901		3950
SEQ_183	3920	ATCACC CGCCATTTCGCAAGCGGATTGAGGAAATCAACGCCCAAAGGCATTC	3969
G_kaustophilu	3951		4000
SEQ_183	3970	AGGCGACGGCGAAAGAAAAAGCTTGCTCACGGTTCTTGAGGTGGCCTTA	4019
G_kaustophilu	4001		4050
SEQ_183	4020	GAGATGTGCGAGCGCGGCTTTTCCTTTAAAAATATCGATTGTACCGCTC	4069
G_kaustophilu	4051		4100
SEQ_183	4070	GCAGGCGACGGAATTCGTCATTGACGGCAATTCTCTCATTCGCGCGTTCA	4119
G_kaustophilu	4101		4150
SEQ_183	4120	ACGCCATTCCGGGGCTTGGGACGAACGTGGCGCAGGCGATCGTGCGCGCC	4169
G_kaustophilu	4151		4200
SEQ_183	4170	CGCGAGGAAGGCGAGTTTTTGTGCGAAGGAGGATTTGCAACAGCGCGGCAA	4219
G_kaustophilu	4201		4250
SEQ_183	4220	ATTGTGCAAAACGCTGCTCGAGTATCTAGAAAGCCGCGGCTGCCTTGACT	4269
G_kaustophilu	4251		4300
SEQ_183	4270	CGCTTCCAGACCATAACCAGCTGTCGCTGTTT	4301
G_kaustophilu	4301		4335

## **Exhibit 3**



# CLUSTAL W (1.83) Multiple Sequence Alignments

Sequence format is Pearson

Sequence 1: SEQ\_184 1433 aa

Sequence 2: G\_kaustophilus 1444 aa

Start of Pairwise alignments

Aligning...

Sequences (1:2) Aligned. Score: 99

Guide tree file created: [/ebi/extserv/clustalw-work/interactive/clustalw-20060823-22024725.dnd]

Start of Multiple Alignment

There are 1 groups

Aligning...

Group 1: Sequences: 2 Score:31068

Alignment Score 8866

CLUSTAL-Alignment file created [/ebi/extserv/clustalw-work/interactive/clustalw-20060823-22024725.aln]

```

SEQ_184      -----MVTKEQKERFLILLEQLKMTSDEWMPHFREAAIRKVVIDKEEKSWHFYFQ 50
G_kaustophilus MMLRGEQTDVMVTKEQKERFLILLEQLKMTSDEWMPHFREAAIRKVVIDKEEKSWHFYFQ 60
                *****

SEQ_184      FDNVLPVHVYKTFADRLQTAFRHIAAVRHTMEVEAPRVTEADVQAYWPLCLAEIQEGMSP 110
G_kaustophilus FDNVLPVHVYKTFADRLQTAFRHIAAVRHTMEVEAPRVTEADVQAYWPLCLAEIQEGMSP 120
                *****

SEQ_184      LVDWLSRQTPPELKGNKLLVVARHEAEALAIKRRFAKKIADVYASFGFPPLQLDVSVEPSK 170
G_kaustophilus LVDWLSRQTPPELKGNKLLVVARHEAEALAIKRRFAKKIADVYASFGFPPLQLDVSVEPSK 180
                *****

SEQ_184      QEMEQFLAQKQOEDEERALAVLTDLAREEEKAASAPPSGPLVIGYPIRDEEPVRRLETIV 230
G_kaustophilus QEMEQFLAQKQOEDEERALAVLTDLAREEEKAASAPPSGPLVIGYPIRDEEPVRRLETIV 240
                *****

SEQ_184      EEERRVVVQGYVFDAEVSELKSGRTLLTMKITDYTNSILVKMFSDRKEDAELMSGVKKGM 290
G_kaustophilus EEERRVVVQGYVFDAEVSELKSGRTLLTMKITDYTNSILVKMFSDRKEDAELMSGVKKGM 300
                *****

SEQ_184      WVKVRGSVQNDTFVRDLVIIANDLNEIAANERQDTAPEGEKRVELHLHTPMSQMDAVTSV 350
G_kaustophilus WVKVRGSVQNDTFVRDLVIIANDLNEIAANERQDTAPEGEKRVELHLHTPMSQMDAVTSV 360
                *****

SEQ_184      TKLIEQAKKWGHPAIAVTDHAVVQSFPEAYSAAKKHGMKVIYGLEANIVDDGVPIAYNET 410
G_kaustophilus TKLIEQAKKWGHPAIAVTDHAVVQSFPEAYSAAKKHGMKVIYGLEANIVDDGVPIAYNET 420
                *****

SEQ_184      HRRLSEETYVVFDEVETTGLSAVYNTIIELAAVKVVDGEIIDRFMSFANPGHPLSVTTMEL 470
G_kaustophilus HRRLSEETYVVFDEVETTGLSAVYNTIIELAAVKVVDGEIIDRFMSFANPGHPLSVTTMEL 480
                *****

SEQ_184      TGITDEMVKDAPKPDDEVLARFVDWAGDATLVAHNASFDIGFLNAGLARMGRGKIANPVID 530
G_kaustophilus TGITDEMVKDAPKPDDEVLARFVDWAGDATLVAHNASFDIGFLNAGLARMGRGKIANPVID 540
                *****;*****

SEQ_184      TLELARFLYPDLKNHRLNTLCKKFDIELTQHHRAIYDAEATGHLLMRLLKEAEERGILFH 590
G_kaustophilus TLELARFLYPDLKNHRLNTLCKKFDIELTQHHRAIYDAEATGHLLMRLLKEAEERGILFH 600
                *****

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SEQ_184	DELNSRTHSEASYRLARPFHVTLQAQNETGLKNLFKLVSLSHIQYFHRVPRIPRSVLVKH	650
G_kaustophilus	DELNSRTHSEASYRLARPFHVTLQAQNETGLKNLFKLVSLSHIQYFHRVPRIPRSVLVKH	660
*****		
SEQ_184	RDGLLVGSGCDKGELFDNLIQKAPEEVEDIARFYDFLEVHPPDVYKPLIEMDYVKDEEMI	710
G_kaustophilus	RDGLLVGSGCDKGELFDNLIQKAPEEVEDIARFYDFLEVHPPDVYKPLIEMDYVKDEEMI	720
*****		
SEQ_184	KNIIRSIVALGEKLDIPVVATGNVHYLNPEDKIYRKILIHSSQGGANPLNRHELDPVYFRT	770
G_kaustophilus	KNIIRSIVALGEKLDIPVVATGNVHYLNPEDKIYRKILIHSSQGGANPLNRHELDPVYFRT	780
*****		
SEQ_184	TNEMLDCFSFLGPEKAKEIVVDNTQKIASLIGDVKPIKDELYTPRIEGADEEIREMSYRR	830
G_kaustophilus	TNEMLDCFSFLGPEKAKEIVVDNTQKIASLIGDVKPIKDELYTPRIEGADEEIREMSYRR	840
*****		
SEQ_184	AKEIYGDPLPKLVEERLEKELKSIIGHGFAVIYLIHSHKLVKKSLLDDGYLVGSRGSGVSSSF	890
G_kaustophilus	AKEIYGDPLPKLVEERLEKELKSIIGHGFAVIYLIHSHKLVKKSLLDDGYLVGSRGSGVSSSF	900
*****		
SEQ_184	VATMTEITEVNPLPPHYVCPNCKHSEFFNDGSGVSGFDLPDKNCPRCGTYKKDGHDI PF	950
G_kaustophilus	VATMTEITEVNPLPPHYVCPNCKHSEFFNDGSGVSGFDLPDKNCPRCGTYKKDGHDI PF	960
*****		
SEQ_184	ETFLGFKGDKVPDIDLNFSGEYQPRAHNYTKVLFGEDNVYRAGTIGTVADKTAYGFVKAY	1010
G_kaustophilus	ETFLGFKGDKVPDIDLNFSGEYQPRAHNYTKVLFGEDNVYRAGTIGTVADKTAYGFVKAY	1020
*****		
SEQ_184	ASDHNLELRGAIEID-LAAGCTGVKRTTGQHPGGIIVVPDYMEIYDFTPIQYPADDTSSSEW	1069
G_kaustophilus	ASDHNLELRGAIEIDRLAAGCTGVKRTTGQHPGGIIVVPDYMEIYDFTPIQYPADDTSSSEW	1080
*****		
SEQ_184	RTTHFDHFSIHDLNLLKLDILGHDDPTVIRMLQDLSGIDPKTIPTDDPDVMGIFSSTEPLG	1129
G_kaustophilus	RTTHFDHFSIHDLNLLKLDILGHDDPTVIRMLQDLSGIDPKTIPTDDPDVMGIFSSTEPLG	1140
*****		
SEQ_184	VTPEQIMCNVGTIGIPEFGTRFVRQMLEETRPKTFSELVQISGLSHGTDVWLGN AQELIQ	1189
G_kaustophilus	VTPEQIMCNVGTIGIPEFGTRFVRQMLEETRPKTFSELVQISGLSHGTDVWLGN AQELIQ	1200
*****		
SEQ_184	NGTCTLSEVIGCRDDIMVYLIYRGLEPSLAFKIMESVRKGKGLTPEFEAEMRKHDVPEWY	1249
G_kaustophilus	NGTCTLSEVIGCRDDIMVYLIYRGLEPSLAFKIMESVRKGKGLTPEFEAEMRKHDVPEWY	1260
*****		
SEQ_184	IDSCKKIKYMFPAHAAAYVLMVAVRIAYFKVHHPLLYYASYFTVRAEDFDLDAMIKGSPA	1309
G_kaustophilus	IDSCKKIKYMFPAHAAAYVLMVAVRIAYFKVHHPLLYYASYFTVRAEDFDLDAMIKGSAA	1320
*****		
SEQ_184	IRKRIEEINAKGIQATAKEKSLTTLVLEVALEMCERGFSEFNIDLYRSQATEFVIDGNSLI	1369
G_kaustophilus	IRKRIEEINAKGIQATAKEKSLTTLVLEVALEMCERGFSEFNIDLYRSQATEFVIDGNSLI	1380
*****		
SEQ_184	PPFNAIPGLGTNVAQAIVRAREEGEFLSKEDLQQRGKLSKTLLEYLESRGCLDSLDPHNQ	1429
G_kaustophilus	PPFNAIPGLGTNVAQAIVRAREEGEFLSKEDLQQRGKLSKTLLEYLESRGCLDSLDPHNQ	1440
*****		
SEQ_184	LSLF	1433
G_kaustophilus	LSLF	1444
***		